

WHAT IS CLAIMED IS:

1. A method of reducing nephrotoxicity in an individual during radioimmunotherapeutic treatment of a pathophysiological condition, comprising:

5 administering a pharmacologically effective dose of at least one adjuvant effective for preventing accumulation of a metal in kidneys;

administering an actinium-225 radioimmunoconjugate to treat the pathophysiological condition; and

10 preventing accumulation of alpha particle-emitting daughters of said actinium-225 within the kidneys of the individual via interaction between said adjuvant and said ²²⁵Ac daughters or the kidney tissue or a combination thereof thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

15 2. The method of claim 1, wherein said adjuvant(s) is administered prior to administering said actinium-225 radioimmunoconjugate, said adjuvant(s) continuing to be administered after said actinium-225 radioimmunoconjugate.

20 3. The method of claim 1, wherein said adjuvant is a chelator, a diuretic, a competitive metal blocker, or a combination thereof.

4. The method of claim 3, wherein said chelator is 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

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5. The method of claim 3, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex or other loop diuretic.

6. The method of claim 3, wherein said competitive metal
10 blocker is bismuth subnitrate or bismuth subcitrate.

7. The method of claim 1, wherein said ^{225}Ac daughter is bismuth-213, francium-221 or a combination thereof.

15 8. The method of claim 1, wherein said actinium-225 radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

9. The method of claim 8, wherein said actinium-225
20 radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

10. The method of claim 1, wherein said pathophysiological

condition is a cancer or an autoimmune disorder.

11. The method of claim 1, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

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12. The method of claim 11, wherein said cancer is myeloid leukemia.

13. A method of reducing nephrotoxicity in an individual during
10 radioimmunotherapeutic treatment a pathophysiological condition, comprising:
administering a pharmacologically effective dose of a chelator;
administering an actinium-225 radioimmunoconjugate to treat the
cancer; and
preventing accumulation of bismuth-213 daughters of said
15 actinium-225 within the kidneys of the individual by scavenging thereof with said
chelator thereby reducing nephrotoxicity during the radioimmunotherapeutic
treatment.

14. The method of claim 13, wherein said chelator is
20 administered prior to administering said ²²⁵Ac radioimmunoconjugate, said
chelator continuing to be administered after said ²²⁵Ac radioimmunoconjugate.

15. The method of claim 13, wherein said chelator is 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

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16. The method of claim 13, further comprising:
administering a pharmacologically effective dose of a diuretic; and
preventing accumulation of francium-211 daughters of said actinium-225 within the kidneys of the individual by inhibiting reabsorption of francium-211
10 therein with said diuretic thereby reducing nephrotoxicity during the radioimmunotherapeutic treatment.

17. The method of claim 16, wherein said diuretic is administered prior to administering said ^{225}Ac radioimmunoconjugate, said
15 diuretic continuing to be administered after said ^{225}Ac radioimmunoconjugate.

18. The method of claim 16, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

20 19. The method of claim 13, wherein said ^{225}Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

20. The method of claim 19, wherein said ^{225}Ac radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

5 21. The method of claim 13, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

22. The method of claim 21, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

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23. The method of claim 22, wherein said cancer is myeloid leukemia.

24. A method of reducing nephrotoxicity in an individual during
15 radioimmunotherapeutic treatment of a pathophysiological condition, comprising:

administering a pharmacologically effective dose of a diuretic;

administering an actinium-225 radioimmunoconjugate to treat the cancer; and

20 preventing accumulation of francium-211 daughters of said actinium-225 within the kidneys of the individual by inhibiting reabsorption of francium-211 therein with said diuretic thereby reducing nephrotoxicity during

the radioimmunotherapeutic treatment.

25. The method of claim 24, wherein said diuretic is administered prior to administering said ^{225}Ac radioimmunoconjugate, said
5 diuretic continuing to be administered after said ^{225}Ac radioimmunoconjugate.

26. The method of claim 24, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

10 27. The method of claim 24, wherein said ^{225}Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a monoclonal antibody.

28. The method of claim 27, wherein said ^{225}Ac
15 radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

29. The method of claim 24, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

20 30. The method of claim 29, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

31. The method of claim 30, wherein said cancer is myeloid leukemia.

32. A method of improving radioimmunotherapeutic treatment
5 of cancer in an individual, comprising:
administering a pharmacologically effective dose of a chelator;
administering an actinium-225 radioimmunoconjugate; and
scavenging bismuth-213 daughters of the actinium-225 with said
chelator to reduce nephrotoxicity in the individual during the treatment thereby
10 increasing the therapeutic index of the actinium-225 to improve the treatment for
said cancer.

33. The method of claim 32, wherein said chelator is
administered prior to administering said ²²⁵Ac radioimmunoconjugate, said
15 chelator continuing to be administered after said ²²⁵Ac radioimmunoconjugate.

34. The method of claim 32, wherein said chelator is 2,3
dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid,
diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid,
20 or zinc diethylenetriamine pentaacetic acid.

35. The method of claim 32, further comprising:

administering a pharmacologically effective dose of a diuretic; and
inhibiting renal uptake of francium-211 daughters of the actinium-
225 with said diuretic to reduce nephrotoxicity in the individual during the
treatment thereby increasing the therapeutic index of the actinium-225 to
5 improve the treatment for said cancer.

36. The method of claim 35, wherein said diuretic is
administered prior to administering said ^{225}Ac radioimmunoconjugate, said
diuretic continuing to be administered after said ^{225}Ac radioimmunoconjugate.
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37. The method of claim 35, wherein said diuretic is
furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

38. The method of claim 35, wherein said ^{225}Ac
15 radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a
monoclonal antibody.

39. The method of claim 38, wherein said ^{225}Ac
radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.
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40. The method of claim 35, wherein said cancer is a solid
cancer, a disseminated cancer or a micrometastatic cancer.

41. The method of claim 40, wherein said cancer is myeloid leukemia.

5 42. A method of improving radioimmunotherapeutic treatment of cancer in an individual, comprising:

administering a pharmacologically effective dose of a diuretic;

administering an actinium-225 radioimmunoconjugate; and

10 inhibiting renal uptake of francium-211 daughters of the actinium-225 with said diuretic to reduce nephrotoxicity in the individual during the treatment thereby increasing the therapeutic index of the actinium-225 to improve the treatment for said cancer.

43. The method of claim 42, wherein said diuretic is
15 administered prior to administering said ²²⁵Ac radioimmunoconjugate, said diuretic continuing to be administered after said ²²⁵Ac radioimmunoconjugate.

44. The method of claim 42, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

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45. The method of claim 42, wherein said ²²⁵Ac radioimmunoconjugate comprises an actinium-225 bifunctional chelant and a

monoclonal antibody.

46. The method of claim 45, wherein said ^{225}Ac radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

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47. The method of claim 42, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

48. The method of claim 47, wherein said cancer is myeloid
10 leukemia.

49. A method of increasing the therapeutic index of an actinium-225 radioimmunoconjugate during treatment of a pathophysiological condition in an individual comprising:

15 inhibiting renal uptake of at least one alpha particle-emitting daughter of actinium-225 whereby nephrotoxicity is reduced during the treatment thereby increasing the therapeutic index of said actinium-225 radioimmunoconjugate.

20 50. The method of claim 49, wherein inhibiting renal uptake of said ^{225}Ac daughter(s) comprises:

administering a pharmacologically effective amount of an adjuvant

comprising:

a chelator to scavenge said ^{225}Ac daughters therewith; or

a diuretic to inhibit reabsorption of said ^{225}Ac daughters within a kidney; or

5 a competitive metal blocker to prevent binding of said ^{225}Ac daughters within a kidney; or

a combination thereof.

51. The method of claim 50, wherein said chelator and/or said
10 diuretic and/or said competitive metal blocker are administered prior to treatment with said actinium-225 radioimmunoconjugate, said chelator and/or said diuretic continuing to be administered after said actinium-225 radioimmunoconjugate is administered to the individual.

15 52. The method of claim 50, wherein said chelator is 2,3 dimercapto-1-propane sulfonic acid, meso 2,3-dimercapto succinic acid, diethylenetriamine pentaacetic acid, calcium diethylenetriamine pentaacetic acid, or zinc diethylenetriamine pentaacetic acid.

20 53. The method of claim 50, wherein said diuretic is furosemide, chlorthiazide, hydrochlorothiazide, bumex, or other loop diuretic.

54. The method of claim 50, wherein said competitive metal blocker is bismuth subnitrate or bismuth subcitrate.

55. The method of claim 50, wherein said chelator scavenges
5 the ^{225}Ac daughter bismuth-213.

56. The method of claim 50, wherein said diuretic inhibits reabsorption of the ^{225}Ac daughter francium-211.

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57. The method of claim 50, wherein said competitive metal binder prevents binding of the ^{225}Ac daughter bismuth-213.

58. The method of claim 49, wherein said actinium-225
15 radioimmunoconjugate is [^{225}Ac] DOTA-HuM195.

59. The method of claim 49, wherein said pathophysiological condition is a cancer or an autoimmune disorder.

20 60. The method of claim 59, wherein said cancer is a solid cancer, a disseminated cancer or a micrometastatic cancer.

61. The method of claim 60, wherein said cancer is myeloid leukemia.